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BRIEF REPORT
Contamination of Poliovirus Vaccine With SV40 and the Incidence of Medulloblastoma

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Simian virus 40 (SV40) contaminated the poliovirus vaccines used throughout the United States and much of the world during the late 1950s and early 1960s. By 1961 in the United States almost 90% of children had received at least one immunization containing SV40, and worldwide many millions of individuals were similarly exposed [1]. This contamination has remained a source of public health concern because SV40 causes cancer in rodents and can immortalize human cells in vitro [1]. Recently, the concern was heightened by the detection of SV40 DNA sequences in several rare human tumors, including ependymomas and choroid plexus tumors (two brain tumors primarily affecting young children), osteosarcomas, and mesotheliomas [2–4]. Epidemiologic investigations conducted over the past several decades, however, have generally failed to detect increased risks of cancer among individuals exposed to SV40 through contaminated vaccine [5,6]. Most recently, a comprehensive study of vaccine-exposed birth cohorts revealed no excess risk of tumors putatively related to SV40, based on more than 30 years of cancer surveillance data in the U.S. [7].

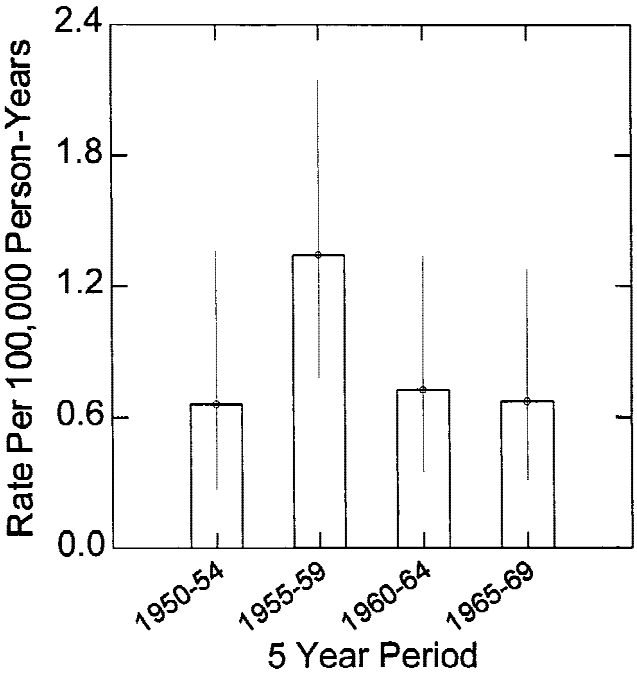

Fig. 1. Medulloblastoma incidence rates in children 0–4 years of age in Connecticut, ''before'' (1950–54), ''during'' (1955–59 and 1960–64), and ''after'' (1965–69) widespread exposure to SV40-contaminated poliovirus vaccine among infants and children. The bars show the calculated medulloblastoma incidence rates, and the central lines depict the 95% confidence limits around these estimates.

One of the few conflicting epidemiologic observations was reported by Farwell et al. [8,9], suggesting that the period of widespread vaccine contamination in Connecticut was associated with increased rates of medulloblastoma, a brain tumor that mainly affects children under 5 years of age. These data are particularly relevant because Connecticut is the only state in the United States that had a well-established tumor registry during the period of vaccine contamination.

To further evaluate this finding, we re-examined the incidence of medulloblastoma cases reported to the Connecticut Cancer Registry in the periods ''before'', ''during'' (1955–1963, but we include 1964 because of latency), and ''after'' distribution of SV40-contaminated poliovirus vaccine. Age-specific rates were calculated for each period using demographic data obtained from the U.S. Bureau of the Census. The trends are presented in Figure 1. Among individuals 0–4 years of age, medulloblastoma incidence showed a non-significant increase ($P = 0.16$) just after immunizations with contaminated vaccine began in 1955. However, the incidence from 1960 through 1964 was similar to the rate during the pre-

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immunization period, 1950–1954. This pattern is important, because cumulative exposure to SV40 was greatest at the end of the contamination period and, given the short latency required for cancers involving very young children, the effect on medulloblastoma incidence was expected to have been greatest during the interval 1960–1964. Similarly, incidence rates among children 5–9 and 10–14 years of age showed no trends related to the use of SV40-contaminated poliovurus vaccine (data not shown.)

Our findings can be reconciled with the earlier studies, by noting that Farwell et al. did not adequately control for age [8,9]. Specifically, they defined ''children'' as individuals less than 20 years of age, without considering that medulloblastoma mainly affects children under 5 years of age and that birth rates rapidly increased during the 1950s. Indeed, the population 0–4 years of age in Connecticut increased about 30% between 1950–1954 and 1960–1964.

We also examined incidence trends for medulloblastoma using data from the Surveillance Epidemiology, and End Results (SEER) program, a representative sample of about 10% of the U.S. population. Because the SEER registry began operations in 1973, cancer incidence data were unavailable for exposed individuals before 9–10 years of age. Our analysis compared the rate of medulloblastoma in selected birth cohorts exposed to SV40-contaminated vaccine as infants (born 1956–1962) or children (born 1947–1952) to the rates in unexposed individuals (born 1964–1969). Specifically, we compared the annualized incidence by individual year of age in the three birth cohorts using Poisson regression. The log-likelihood test was used to select the best-fitting model from a series that treated the age-effect as uniform, linear, quadratic, or as a cubic spline with two or three segments. In the quadratic model that best fit medulloblastoma incidence rates (goodness of fit: 55.35 on 77 df), the risk of medulloblastoma was found to be less ($P = .052$) in the cohorts exposed to SV40-contaminated vaccine as infants (RR = 0.742; 95% CI 0.55–1.00) or children (RR = 0.565; 95% CI 0.34–0.94) as compared to individuals born soon thereafter and never exposed.

In summary, incidence data from the Connecticut Cancer Registry and from the SEER registry have failed to demonstrate increased rates of medulloblastoma in groups exposed to SV40-contaminated poliovirus vaccine as compared to unexposed individuals of similar age. Although SEER data were only available for the exposed groups after 9–10 years of age, they were derived from representative geographic regions to estimate the national experience. Although the Connecticut registry provides more limited geographic representation, the data were available for exposed individuals since birth. We conclude that immunization with SV40-contaminated poliovirus vaccine in infants and children was not associated with increased risk of medulloblastoma. Our data did not permit us to evaluate an additional finding by Farwell et al., that there was increased risk of medulloblastoma among the children born to mothers immunized with contaminated vaccine during pregnancy. That observation requires further study [5], and there should be continued surveillance of the birth cohorts exposed to SV40-contaminated vaccine as they grow older.

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